REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on May 30, 2003, and the references cited therewith. New claims 92 and 93 have been added to further delineate the subject matter to which applicant is entitled. Support for the subject matter of claims 92 and 93 can be found in pending claim 48 and throughout the specification, for example, in the Examples and in Figures 2A, 3A, 4A, 7A and 7B. Applicant submits that addition of claims 92 and 93 has added no new matter to the specification.

§112, Second Paragraph Rejection of the Claims

Claims 48-61 were rejected under 35 USC § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. The Examiner has stated that the claims are vague and indefinite for allegedly failing to set forth salient characteristics (structural details) of each monomer and how they interact to form a trimer.

Claim 48 is drawn to a stabilized viral envelope protein comprising three parallel, α-helical COOH-terminal viral envelope glycoprotein monomers that together form a stable three-stranded coiled coil having a conformation like that of a native form of the viral envelope glycoprotein when associated with a cellular membrane, wherein the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion, and wherein the monomer comprises SEQ ID NO:8.

Indefiniteness depends on whether one of skill in the art would understand the scope of the claim when the claim is read in light of the specification. *North American Vaccine Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 28 USPQ2d 1333 (Fed. Cir. 1993). If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more. *Miles Laboratories Inc. v. Shandon, Inc.*, 997 F.2d 870, 27 USPQ2d 1123 (Fed. Cir. 1993).

Applicant submits that one of skill in the art would clearly understand the scope of the invention as defined by the claims particularly when the claims are read in light of the specification. In particular, the claims particularly point out and distinctly claim specific structural, amino acid sequence and functional features that specify exactly what scope is

intended. Applicant respectfully requests withdrawal of this rejection under 35 USC § 112, second paragraph.

§112, First Paragraph, Rejection of the Claims

Claims 48-61 were rejected under 35 USC § 112, first paragraph, as allegedly lacking written description. The Examiner has alleged that the specification does not provide adequate support for the broadly claimed genus of monomeric peptides. The Examiner has further alleged that the specification discloses only a single trimer of a gp41 monomer fused to a GCN4-pII domain and fails to provide guidance as to acceptable amino acid substitutions.

Contrary to the Examiner's allegations, Applicant provides more than one example of a stabilized viral envelope protein composed of α-helical COOH-terminal viral envelope glycoprotein monomers that have a sequence comprising SEQ ID NO:8. In particular, the specification discloses the C45-pII, C29-p, C-52 and Q652L proteins.

As described at page 23, lines 18-21, the C45-pII protein is a fusion of gp41 residues 624 to 668 (see Fig. 4A) with GCN4-pII, and this C45-pII fusion protein is fully helical in solution (see Fig. 3B and page 25, line 1). Hence the C45-pII fusion protein is a stabilized viral envelope protein that is fully helical in solution.

As described at page 23, line 23 to page 24, line 7, the C29-p protein is a proteolysis product of the C45-pII fusion protein and has gp41 residues 640 to 668 fused to residues 1 to 27 of GNC4-pII. Moreover, the C29-p protein "forms a discrete trimer with 100% helix content."

The C52 peptide containing the entire C45 region plus 7 added residues on the COOH terminal (Fig. 4A) has substantial helical structure and forms a trimer in solution. See Example 3 (page 25, lines 3-20).

The specification further discloses at page 26 that the Q652L peptide is a Gln^{652} to Leu mutant of the C52 peptide. Moreover, the Q652L peptide has substantial helical character and sediments as a trimer at concentrations between 30 and 100 μM (Fig. 6C). Hence, the specification provides several examples of stabilized viral envelope protein comprising three parallel, α-helical COOH-terminal viral envelope glycoprotein monomers that together form a stable three-stranded coiled coil having a conformation like that of a native form of the viral

envelope glycoprotein when associated with a cellular membrane, and wherein the monomer comprises SEQ ID NO:8.

Contrary to the Examiner's allegations, the specification provides ample guidance as to acceptable amino acid substitutions. In particular, the specification teaches which types of mutations in the gp41 peptide monomers can positively and negatively affect the formation of a trimer, for example, in Example 5. Also, Figures 3A and 8 illustrate which amino acids can be used at what positions within the gp41 heptad repeat so that helicity is maintained.

Moreover, the specification teaches that so long as the three parallel, α-helical COOH-terminal viral envelope glycoprotein monomers retain their secondary (helicity) and tertiary (trimer) structures, the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion. See, for example, at page 25, line to page 26, line 12; page 27, lines 14-24. As described, for example, in Examples 5 and 7, circular dichroism and sedimentation equilibrium studies can be used to assess whether the monomers are α-helical and trimeric, respectively. Thermal or chemical denaturation studies can be used to assess the stability of the viral envelope protein (*id.*). The C52-pII protein, for example, is fully helical, has a thermal stability that exceeds 100°C and forms a well-structured and extremely stable, three-stranded coiled coil (page 29, line 20 to page 30, line 11).

Accordingly, the specification provides several species of stabilized viral envelope proteins with the claimed structural and functional features and teaches one of skill in the art how to make sequences variations in those proteins by making amino acid substitutions that will not alter the claimed features.

Applicants submit that the claims describe the claimed invention with all of its limitations using such descriptive means as words, structures, and formulas that fully set forth the claimed invention. In particular, the claims identify specific sequences for stabilized viral envelope proteins that can have three parallel, α-helical COOH-terminal viral envelope glycoprotein monomers, which have a sequence comprising SEQ ID NO:8, wherein the stabilized viral envelope protein is substantially incapable of undergoing a conformational change to become active for membrane fusion. Applicants have therefore shown that they were in possession of the invention at the time of filing by describing several actual reductions to practice.

Moreover, Applicants submit that the Written Description Guidelines do not even require that applicants disclose every detail of the claimed invention. The "Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, P1, 'Written Description' Requirement," 66 Fed. Reg. 1099, 1099 (Jan. 5, 2001)("Guidelines") state as follows:

> To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.

66 Fed. Reg. at 1104. The Guidelines also provide guidance as to how the written description requirement can be satisfied.

> An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

Id.

Moreover, contrary to the Examiner's allegations, Applicants need not describe every nuance of the invention in order to satisfy the written description requirement.

> What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.

Guidelines at 1106.

Accordingly, Applicants have provided a description showing that the inventors were in possession of the invention and respectfully request withdrawal of this written description rejection under 35 U.S.C. § 112, first paragraph.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (516-795-6820) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

MIN LU ET AL.,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 26th day of August, 2003.

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